The Transmissibility of the Spanish Flu Pandemic in Geneva, Switzerland

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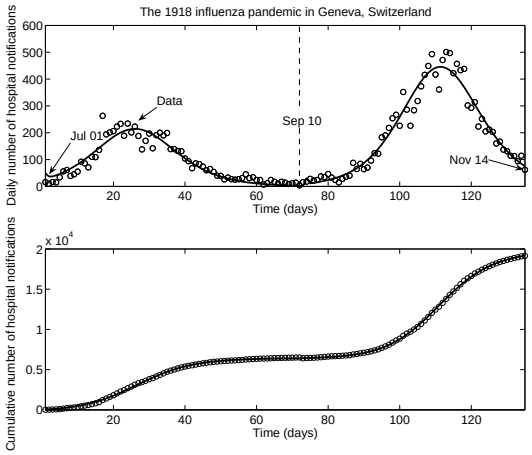
The transmissibility of infectious diseases can be quantified by the number of secondary cases generated by a primary infectious case in an entirely susceptible population or basic reproductive number [3]. In the context of recurrent or endemic diseases such as influenza, the reproductive number accounts for the residual immunity in the population due to previous exposures or vaccination campaigns. We estimate the reproductive number of the 1918 influenza pandemic (Spanish flu) in the Canton of Geneva, Switzerland using a compartmental epidemic model. The uncertainty of model parameters was determined via a simulation study. We estimate the basic reproductive number for the first wave to be 1.49 (95% confidence interval (CI): 1.45-1.53) and the reproductive number for the second wave to be 3.75 (95% CI: 3.57-3.93). In addition, we estimate the clinical reporting rate for these two waves to be 59.7% (95% CI: 55.7-63.7) and 83% (95% CI: 79-87). We surmise that the lower reporting rate in the first wave can be explained by a lack of initial awareness of the epidemic and the relative higher severity of the symptoms experienced during the second wave. Our findings indicate that intervention strategies aiming at reducing transmission from hospital settings when implemented alone are unlikely to achieve control unless combined with a reduction in the susceptibility of the general population. We found that reductions in the susceptibility of the general population (for the second wave of infection) through increasing hygiene and protective measures, prophylactic antiviral use, and vaccination are more effective and our model predicts control when these reductions are greater than 77%. Control is more feasible when both interventions strategies are implemented simultaneously. For example, our model predicts that a reduction of 50% or greater in the susceptibility of the general population and a reduction of 65% or greater in transmission from hospital wards would guarantee control.

The 1918/9 influenza pandemic affected more than 50% of the population in Geneva, Switzerland [1]. The first wave occurred in July 1918 and the second wave was the deadliest during October-November 1918, and the third wave was observed at the end of 1918 ("winter wave").

Daily epidemic data for the Canton of Geneva was obtained from the mandatory notifications registry in Switzerland [1]. The total number of hospitalized cases during the the Spanish flu in Geneva was 21754 cases (12.45% of total population) with an overall case fatality proportion of 4.2% [1]. The second influenza wave is well documented to have been much deadlier than the first wave [1].

We model the first two waves of the 1918 influenza pandemic in Geneva, Switzerland (Figure 1) separately using a compartmental epidemic model. The model (Figure 2) for the transmission dynamics of pandemic influenza classifies individuals as susceptible (S), exposed (E), clinically ill and infectious (I), asymptomatic and partially infectious (A), hospitalized and reported (J), recovered (R), and death (D). We assume that the birth and natural death rates have common rate μ and that the population is completely susceptible to the first wave of infection. Individuals that recover during the first wave are assumed protected to the second wave [2]. Susceptible individuals in contact with the virus progress to the latent class at the rate $\beta(I(t)+J(t)+qA(t))/N(t)$ where β is



The best fit model solution (solid) to the daily and cumulative number of hospital notifications during the first two waves of the 1918 influenza pandemic (circles) in Geneva, Switzerland.

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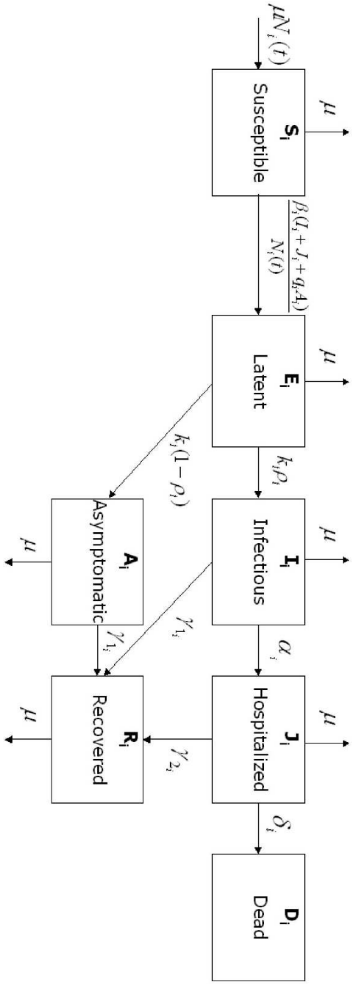

Flow chart of the state progression of individuals among the different epidemiological classes.

the transmission rate, and $0 < q < 1$ is a reduction factor in the transmissibility of the asymptomatic class (A). Since there is no evidence of the effectiveness of interventions, and disruptions in the sanitary and medical sectors were common [1], hospitalized individuals (J) are assumed infectious. Hence, the total population size at time t is given by $N(t) = S(t) + E(t) + I(t) + A(t) + J(t) + R(t)$. We assumed homogeneous mixing between individuals and, therefore, the fraction $(I(t) + J(t) + qA(t))/N(t)$ is the probability that a random contact would be with an infectious individual. A proportion $0 < \rho < 1$ of latent individuals progress to the clinically infectious class (I) at the rate k while the rest $(1-\rho)$ progress to the asymptomatic partially infectious class (A) at the same rate k. Asymptomatic cases progress to the recovered class at the rate γ_1. Clinically infectious individuals (class I) are hospitalized (reported) at the rate α or recover without being diagnosed (e.g., mild infections, hospital refusals [1]) at the rate γ_1. Hospitalized individuals (reported) recover at the rate $\gamma_2 = 1/(1/\gamma_1 - 1/\alpha)$ or die at rate δ. The mortality rates were adjusted according to the case fatality proportion (CFP) such that $\delta = \frac{CFP}{1-CFP}(\mu+\gamma_2)$ (see Figure 2).

A formula of the reproductive number (not shown) can be obtained using standard methods in mathematical epidemiology [4]. Model parameters were estimated using least-square fitting techniques, and the associated parameter uncertainty was obtained via parametric bootstrapping (see ref. [5]). There is evidence of early herald waves of influenza in 1916 prior to the 1918/9 pandemic characterized by high mortality in the young [6]. The first wave of infection for the situation in Geneva, Switzerland seems to resemble the dynamics of annual outbreaks of influenza as indicated by its small basic reproductive number. Today, the identification of these "early" outbreaks could give us more time to prepare for the coming pandemic by increasing the stockpiles of antivirals and possibly the preparation of new vaccines. This highlights the importance of maintaining global virological surveillance for influenza viruses to obtain information about future pandemic viruses that could aid in the elaboration of new vaccines. Rapid identification of emerging viruses can extend the time available from the appearance of the "early" herald waves to the actual pandemic waves. This is increasingly important and challenging because of our expanding highly interconnected worldwide transportation networks.

References

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